Using a Life-Stage Approach for Assessment of Children's Health Risk

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Science Question

What is the basis for differential risk? What are the outcomes that need to be considered in a life-stage focused risk assessment framework? What is the impact of exposure to environmental hollutants throughout development on human health what is the basis for amerental insk? What are the outcomes that need to be considered in a file-stage focused risk assessment framework? What is the impact of exposure to environmental pollutants throughout development on human health outcomes? How do we incorporate data on susceptible populations into the risk assessment process?

Research Goals

Incorporate into risk assessment a focus on life stage-specific considerations for exposure and effects in order to better characterize the risk to susceptible groups within the population.

Reproductive Age Adult

Results/Conclusions

Summary of gap analysis:

·Identify needs for specific areas for guidance

·Application of developmetal and reproductive outcomes to risk assessments for various durations.

·Dose-response assessment for developmental data

·Pharmacokinetic modeling.

·Life-stage specific application of mode of action to risk assessment

·Identify training needs and training tools.

Problem Formulation

Prenatal Risk Infant Risk

Hazard Characterization

Available studies
 Life stage-specific exposures assessments, and outcomes

• Consider

Uncertainties

Summarize the database

Scoping of Hazard

Review Individual Studies · Study purpose, design, and exposures

. Toxicokinetics & toxicodynamics (MOA)

Characterization the Hazard Database

Conduct weight-of-evidence assessment:

. Uncertainties and data gaps Extent of the database

Life stage-specific outcomes

 Scientific Rationale · Sensitivity / specificity

Uncertainty

 Control of confounders, effect modifiers Toxicokinetics; toxicodynamics (MOA)

· Interspecies comparisons of outcomes Relevance of animal data to humans

Qualitative dose-response relationships for adverse outcomes

Impact and Outcomes

This framework addresses the question of why and how an improved children's health risk assessment will strengthen the overall risk assessment process across the Agency. The value added of this approach includes:

1) A more complete evaluation of the potential for vulnerability at different life

- stages,
 2) Evaluation of potential for toxicity after exposure during all developmental 2) Evaluation of potential for toxicity arrei exposure coming the stages,
 3) Integration of adverse health effects and exposure information across life stages, and
 4) A focus on the underlying biological events and critical developmental periods for incorporating mode of action considerations.

Future Directions

- Get Framework externally reviewed
 Develop chemical specific case studies
- Develop criemical specific case studies
 Develop adjunct guidance where needed
 Develop training for Program Offices and other risk assessors
 Apply life stage-specific approach in future assessments.

Exposure Assessment

Pathways (media and route)

Consider

Sources

Scenarios

Select Approach

Screening Approach

Refined Assessment

Scientific Rationale
 Variability

· Sensitivity analysis

Uncertainty

Scoping of Exposure Assessment

Review Available Data

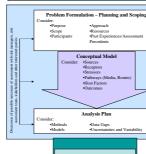
Life Stage-Specific Exposure Analysis

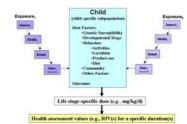
Life Stage-Specific Exposure

· Exposure Media Concentrations

Life Stage-Specific Population Characteristics

Life Stage-Specific Activity Data





Analysis

Dose-Response



Select Dose-Response Relationship(s)

 Summarize dose-response relationships
 Conceptualize the MOA/Identify dose metric Select life stage-specific D-R models (if available) or compile necessary life stag

Extrapolation & Risk Value Derivation

specific physiological parameter data

- Adjust PODs for route, duration, intraspecies, and interspecies factors and/or run PBTK and BBDR models with life stage-specific eter adjustments Derive risk value(s)
- Adjust risk values by appropriate UFs

Life Stage-Specific Dose-Response

- Scientific Rationale
- Uncertainty

Risk Characterization

Synthesis of and integration of hazard, dose response and exposure information

Summary of uncertainties and assumptions used in assessment including variability and uncertainty in database

Describe risk context.







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